



Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Antivirals (Antiherpetic Agents)

Overview:

The antiviral agents discussed in this review are used to treat infections caused by herpes simplex viruses (HSV) and varicella-zoster viruses (VZV). Two types of HSV exist: HSV-1 and HSV-2. Both HSV are serious human pathogens in the herpes family. Among the two, HSV-1 is normally associated with orofacial infections and encephalitis; HSV-2 is usually the cause for genital herpes. More than one in five Americans (45 million people) is infected with genital herpes. Varicella-zoster viruses cause two different diseases: chickenpox, which typically occurs in children, and shingles (herpes zoster), which occurs in elderly or immunocompromised people. Over 90% of adults in the U.S. have serologic evidence of VZV. The annualized incidence of herpes zoster is about 1.5-3.0 cases per 1000 persons.

Acyclovir, famciclovir, and valacyclovir are three oral antiherpetic virus agents available in the U.S. Valacyclovir and famciclovir are prodrugs, which convert to acyclovir and penciclovir, respectively. Acyclovir, famciclovir, and valacyclovir are nucleoside analogues, which competitively inhibit viral DNA polymerase and further inhibit viral replication. The inhibitory activity of these agents is highly selective. These agents must be activated by the enzyme thymidine kinase, which is encoded by HSV and VZV. These drugs have limited efficacy against cytomegalovirus (CMV) and Epstein-Barr virus (EBV) and are not effective against the human immunodeficiency virus.

The efficacy profiles are similar among these three agents. Acyclovir was the first antiherpetic virus agent and is available in a variety of dosage forms. All dosage forms of acyclovir have generically equivalent products; famciclovir is also available generically. Valacyclovir and famciclovir are newer agents that provide a more convenient dosing schedule, and these agents are indicated for the treatment of cold sores. Based on the CDC guidelines, acyclovir should be administered three to five times daily, famciclovir two to three times daily, and valacyclovir one to two times daily for the treatment of genital herpes. However, famciclovir and valacyclovir do not offer additional antiviral coverage against acyclovir resistant strains, which may occur in immunocompromised patients. Currently, acyclovir resistance emerging among immunocompetent patients is not significant.



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The treatment for the first or recurrent episodes of HSV or VZV infections should be initiated immediately after the onset of symptoms in order to achieve the maximum effect. Data on the

safety or effectiveness of chronic suppressive therapy for more than one year's duration with famciclovir and valacyclovir are not available. For acyclovir, the need for continuation of therapy should be evaluated after one year of therapy.

Generic Name	Brand Name	Manufacturer	Generic Available
Acyclovir	Zovirax [®]	GlaxoSmithKline, various	Yes
Famciclovir	Famvir [®]	Novartis	Yes
Valacyclovir	Valtrex [®]	GlaxoSmithKline	Yes

Summary:

The efficacy of acyclovir, famciclovir, and valacyclovir against HSV and VZV infections was similar based on several comparative studies. The CDC guidelines suggest all three antiherpetic virus agents could be used for the treatment and suppression of genital herpes. The difference in these three agents is the dosing schedule, with newer agents offering more convenient dosing. In addition, all three agents are available generically. Selection of one agent for the preferred drug list should provide sufficient coverage for patients with HSV or VZV infections.